Physical activity habits, limitations and predictors in people with inflammatory bowel disease: a large cross-sectional online survey

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Abstract

Background: Limited evidence suggests that physical activity has beneficial effects in people with inflammatory bowel disease (IBD). This study aimed to determine the physical activity habits of adults with IBD, the limitations to physical activity they experience because of their disease, and the extent to which their physical activity is affected by various demographic, clinical and psychological factors.

Methods: Data were collected on 859 adult participants (52% with Crohn's disease [CD], 75% female) via an online survey conducted between May and June 2016. Measures included physical activity (International Physical Activity Questionnaire), psychological symptoms (Hospital Anxiety and Depression Scale), fatigue (sub-items of IBD fatigue scale), exercise perceptions (Exercise Benefits/Barriers Scale) and disease activity. Regression analyses were used to identify predictors of physical activity.

Results: Only 17% of respondents were categorised as "high active". Self-reported physical activity levels decreased, and fatigue and psychological scores increased, with increasing disease activity. Walking was the most common activity performed (57% of respondents) and running/jogging the most commonly avoided (34%). Many participants (n=677) reported that IBD limited their physical activity for reasons including abdominal/joint pain (70%), fatigue/tiredness (69%), disease flare-up (63%), and increased toilet urgency (61%). Physical activity was independently associated with depression, disease activity and perceived barriers to exercise in people with CD, and depression and age in people with ulcerative or indeterminate colitis (all $P \leq 0.038$).

Conclusions: This survey highlights several important factors that should be considered by designers of future physical activity interventions for people with IBD.

Key Words: Crohn's disease; exercise; depression; fatigue; physical activity; ulcerative colitis

1. Introduction

Physical activity and exercise are important lifestyle behaviours for the general population: they are associated with improvements in physical fitness and mental well-being (1, 2); they facilitate weight management (3); and, independently of these benefits, they have been associated with lower mortality rates (4). Physical activity/exercise may also be a useful adjunctive therapy for people with inflammatory bowel disease (IBD) by improving immune function and mood, reducing fatigue, and promoting gains in muscle and bone strength (5). However, the evidence for physical activity/exercise in IBD is sparse, with only a handful of intervention studies (6-9), some of which have methodological limitations such as short follow-up, no control group, and a small sample size. As such, it is perhaps unsurprising that there are currently no evidence-based physical activity guidelines that are specific to IBD.

Despite the numerous potential benefits of physical activity, there is evidence that a large proportion of the IBD population is physically inactive, and that people with IBD are less active than people without IBD (10, 11). Although the reasons for this are unclear, recent surveys have demonstrated that many patients cite limitations to physical activity due to IBD-related factors such as fatigue, joint pain, and lack of toilet access (12, 13). There is also evidence from other populations that depression disorders and symptoms, which have a reported prevalence in IBD of 15.2% and 21.6%, respectively (14), may have an adverse impact on self-management behaviours such as physical activity (15). A better understanding of the modifiable correlates of physical activity in people with IBD will aid in the development of interventions with the potential to favourably-modify behavioural and health outcomes.

Given the lack of research in this area, the purpose of this study was to characterise the physical activity habits of adults with IBD, to explore limitations to physical activity that patients may face

65 because of their disease, and to identify factors that are associated with physical activity. An
66 additional objective was to explore clinical and psychological correlates of fatigue.
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2. Materials and Methods

2.1 Ethics approval

The study was approved by the Northumbria University Faculty of Health and Life Sciences Research Ethics Committee in May 2016.

2.2 Design

A cross-sectional online survey was conducted.

2.3 Participants

Participants were a non-clinical population recruited via on-line advertisements on Twitter, Facebook and Instagram. They were invited to participate if they had a formal diagnosis of IBD and were at least 18 years of age. Respondents who were younger than 18 years old were excluded.

2.4 Procedure

The survey was conducted between May and June 2016. The link to the survey was included in the advertisements and interested respondents answered the survey directly through this link. Survey Monkey was used as it allowed confidential access and facilitated data analysis. Study information was provided at the commencement of the survey, and respondents had to provide informed consent before they could participate. Contact details of the researchers were provided in case any queries arose.

2.5 Survey

The survey was anonymous. The first section collected participants' age, gender, employment status, smoking status, and whether they Crohn's disease (CD), ulcerative colitis (UC) or indeterminate colitis (IC). The second section assessed duration of diagnosis, current treatments, surgical history, disease activity, depression and anxiety symptoms, and fatigue. For people with CD, disease activity

was assessed using the PRO3 Index, with scores of <13, 13-21, 22-52 and ≥52 indicative of inactive, mildly active, moderately active, and severely active disease, respectively (16). For people with UC or IC, disease activity was assessed using the Patient-based Simple Clinical Colitis Activity Index (P-SCCAI), with scores of <5 and ≥5 indicative of inactive and active disease, respectively (17). Depression and anxiety symptoms were measured by using the Hospital Anxiety and Depression Scale (HADS) (18). Fatigue was assessed using items 4 and 5 of the IBD Fatigue Scale (19): "What was your AVERAGE fatigue level in the past two weeks?" (5-point ordinal scale ranging 0 [No fatigue] to 4 [Severe fatigue]) and "How much of your waking time have you felt fatigued in the past two weeks" (5-point ordinal scale ranging 0 [None of the time] to 4 [All of the time]). A composite fatigue score was calculated by multiplying the responses to these two questions. The third section of the survey assessed participants' physical activity habits using the International Physical Activity Questionnaire (IPAQ) – Short Form (20). Standard scoring criteria were used (http://www.ipaq.ki.se) to classify respondents as 'inactive', 'minimally active' or 'HEPA active' (health enhancing physical activity; a high activity category). Standard formulae were also used to produce a continuous indicator of physical activity; a total physical activity score in MET-min/week, computed as the sum of walking, moderate, and vigorous MET-min/week scores (http://www.ipaq.ki.se). Participants were also asked to list up to 3 types of physical activity, exercise or sport that they most frequently participated in over the past year, and up to 3 types of physical activity, exercise or sport that they avoided because of their IBD in the past year. The final section of the survey assessed participants' perceived benefits and barriers to exercise using the Exercise Benefits/Barriers Scale (21), and their reasons (if applicable) for IBD limiting participation in physical activity.

2.6 Statistical analysis

All responses collected via Survey Monkey were inspected, downloaded into Excel, coded and analysed using descriptive statistics (means, standard deviations [SD], medians, interquartile ranges [IQR], frequencies, and percentages). All returned surveys were included in the analysis, regardless

of the amount of missing data. Consequently, the number of total responses for each survey item varied due to missing data and refusal/inability to answer.

Multivariable linear regression analyses were conducted to determine the combination of clinical and psychological indices that best explained the observed variations in physical activity and fatigue scores. Separate models were constructed for people with CD and people with UC or IC (combined). Inspection of the total physical score in MET-min/week demonstrated significant positive skew that was transformed to a normal distribution using logarithmic transformation. The fatigue composite score was treated as a continuous outcome, and inspection of the histogram demonstrated an approximately normal distribution.

A multi-stage strategy was used to develop our explanatory models. Firstly, correlation matrices were produced to explore the relationship between dependent variables (physical activity and fatigue) and potential predictor variables (age, gender, disease severity, disease duration, depression, anxiety, exercise barriers score, and exercise benefits score). Indices that demonstrated significant correlation (two-tailed $p<0.05$) with the dependent variable were then carried forward for inclusion in a 'stage 1' multivariable linear regression model. The final model was then constructed, retaining only those coefficients making a significant ($p<0.05$) contribution to the overall model fit. Analyses were conducted using IBM SPSS Statistics Version 22 (IBM United Kingdom Limited, Hampshire, UK).

3. Results

3.1 Participant characteristics

Overall, there were 859 eligible respondents to the survey, of whom 75.2% were female (Table 1). The mean (SD) age was 37.3 (11.6) years, 52% had CD, and the median (IQR) time since diagnosis was 87 (36 to 178) months. According to the PRO3 Index data, 28.3% of people with CD were in clinical remission, and 19.0%, 45.1% and 7.6% had mildly-, moderately-, or severely-active disease, respectively. Using the P-SCCAI data, 40.7% of people with UC or IC had inactive disease, and 59.3% had active disease. Table 2 shows data on current treatments and surgical history.

3.2 Physical activity habits and limitations

Of the 737 respondents who completed the IPAQ, 17.1% were classified as HEPA (i.e., high) active, 49.6% as minimally active, and 33.3% as inactive (Table 3). The median total physical activity was 1866 (594 to 4040) MET·min/week and mean daily sitting time was 429 (225) min. The proportion of physically-inactive individuals increased, in both disease sub-groups, with increasing disease activity. For example, 21.7% of people with mildly-active CD reported being physically inactive versus 62.1% of people with severely-active CD. The exercise barriers scores also increased, and the exercise benefits scores decreased, with increasing disease activity (Table 3).

Figure 1A shows that the respondents had participated in a wide range of activities/exercises in the past year, with walking being the most common activity by far (56.7%). There were no marked differences between disease sub-types. Similarly, the types of activity/exercise that were avoided because of IBD did not differ markedly between CD and UC/IC respondents (Figure 1B). Of the 712 respondents, running/jogging was the most commonly avoided activity (32.2%).

Six hundred and seventy-seven participants (79%) reported that their IBD limited their participation in physical activity/exercise (Figure 2). The most common reasons were abdominal or joint pain (n =

473), fatigue or tiredness (n = 471), disease flare-up (n = 430), and increased toilet urgency (n = 411). The proportion of respondents providing reasons tended to be higher in CD versus UC/IC (e.g., 80.9% vs. 57.1% for abdominal or joint pain; 84.3% vs. 52.7% for fatigue or tiredness).

3.3 Depression, anxiety and fatigue

Of the whole IBD cohort, 33.1% and 22.3% of respondents had abnormal anxiety and depression scores (i.e., HADS scores of 11 to 21), respectively. The anxiety and depression scores were generally higher in CD versus UC/IC, with higher scores also seen in individuals with more-active disease (Table 3).

Data on average fatigue levels in the past two weeks is presented in Figure 3. Fatigue scores were generally worse in people with CD, in females, in people with higher levels of disease activity, and in people with lower levels of physical activity. For example, “severe fatigue” was more frequently reported in people with CD than people with UC/IC (26.8% vs. 20.1%), in females than males (CD: 27.3% vs. 25.5%; UC/IC: 20.8% vs. 11.5%), and in physically-inactive individuals than high-active individuals (CD: 33.8% vs. 19.0%; UC/IC: 38.5% vs. 9.4%).

3.4 Predictors of physical activity and fatigue

Table 4 shows the correlations between physical activity, fatigue and various demographic, clinical and psychological factors. In people with CD, variables that were significantly correlated with logarithmically-transformed total physical activity were disease activity (r = -0.228, P<0.01), depression (r = -0.287, P<0.01), anxiety (r = -0.120, P<0.05), fatigue (r = -0.127, P<0.05), exercise benefits score (r = 0.244, P<0.01), and exercise barriers score (r = -0.292, P<0.01), whereas variables that were significantly correlated with fatigue were duration of diagnosis (r = 0.110, P<0.05), disease activity (r = 0.479, P<0.01), depression (r = 0.538, P<0.01), anxiety (r = 0.465, P<0.01), and physical activity (r = -0.127, P<0.05). In people with UC/IC, variables that were significantly correlated with

194 logarithmically-transformed total physical activity were age (r = -0.158, P<0.01), disease activity (r = -
195 0.123, P<0.05), depression (r = -0.240, P<0.01), fatigue (r = -0.181, P<0.01), and exercise benefits
196 score (r = 0.171, P<0.01) , whereas variables that were significantly correlated with fatigue were
197 disease activity (r = 0.393, P<0.01), depression (r = 0.572, P<0.01), anxiety (r = 0.453, P<0.01), and
198 physical activity (r = -0.181, P<0.01).

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200 The multivariable linear regression models for physical activity and fatigue are shown in Tables 5 and
201 6, respectively. After adjusting for each of the included demographic, clinical and psychological
202 factors, several variables were found to be independently associated with low physical activity levels
203 including higher disease activity (B = -0.010, P=0.038), depression (B = -0.077, P=0.002) and exercise
204 barriers (B = -0.035, P=0.008) scores for people with CD, and higher age (B = -0.016; P=0.011) and
205 depression score (B = -0.053, P=0.025) for people with UC/IC. In the final models, these factors
206 explained 12.3% and 7.3% of the observed variability in self-reported total physical activity in the CD
207 and UC/IC groups, respectively.

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209 Variables that were found to be independently associated with higher fatigue scores were longer
210 time since diagnosis (B = 0.005, P=0.011), and higher disease activity (B = 0.076, P<0.001),
211 depression (B = 0.324, P<0.001) and anxiety (B = 0.183, P=0.001) scores in people with CD, and
212 female gender (B = -1.360; P=0.006), and higher depression (B = 0.454; P<0.001) and anxiety (B =
213 0.180; P=0.003) scores in people with UC/IC. In the final models, these factors explained 37% and
214 36% of the observed variability in self-reported fatigue in the CD and UC/IC groups, respectively.

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4. Discussion

The main novel finding from this cross-sectional online survey was that physical activity was negatively and independently associated with depression, disease activity and exercise barriers in people with CD, and depression and age in people with UC/IC. Other key findings are as follows: the large majority of respondents, regardless of disease type, did not engage in physical activity at levels commensurate with public health guidelines; physical activity levels were lower and fatigue and psychological scores higher in people with higher levels of disease activity; walking was by far the most common type of physical activity performed, with running/jogging the most common activity avoided because of IBD; a large proportion of respondents provided reasons for IBD limiting their participation in physical activity, including pain, fatigue, flare-up and increased toilet urgency, and; independent predictors of fatigue were time since diagnosis, disease activity, depression and anxiety in people with CD, and gender, depression and anxiety in people with UC/IC.

There is a paucity of published data on predictors of physical activity in people with IBD. In a recent study in which 7-day accelerometry was used to objectively measure physical activity in 48 adults with CD, low body mass index (<21 kg/m^2), longer time since diagnosis, presence of systemic inflammation (indicated by serum C-reactive protein >3 mg/L) and low vitamin D3 (<50 nmol/L) were all independently associated with lower physical activity (zero bouts of moderate-to-vigorous physical activity during the 7-day accelerometer-wear period) (11). Unfortunately, the authors did not report how much of the variation in physical activity was explained by these variables. Of these predictor variables, only time since diagnosis was recorded in the current study, and we did not observe a significant association (Table 4). The reason for this discrepancy is unclear, but may be due to differences in the study populations and the way physical activity was measured and classified. In the present study, although large amounts of the variability in total physical activity remained unexplained by the regression models, it was notable that depressed mood emerged as being independently associated with less physical activity in both CD and UC/IC sub-groups. Such an

association, which has previously been reported for adults with type 2 diabetes (22), might be explained by depressed mood having an adverse impact on self-management behaviours (15); however, the evidence from randomised controlled trials is currently equivocal as to whether depression-specific management in depressed individuals leads to increased physical activity (23, 24). We acknowledge that cross-sectional studies cannot assign causality and highlight that the inverse association between physical activity and depressed mood is likely bi-directional (25). Viewed this way, our findings may suggest a potential beneficial effect of regular physical activity on depressive symptoms in people with IBD. A recent meta-analysis of 35 randomised controlled trials (n=1356) showed that exercise training is moderately more effective than a control intervention for reducing symptoms of depression in adults with depression (2); however we are not aware of any prospective trials that have explored the potential mental health benefits of exercise training in people with IBD specifically. Given that a relatively high proportion of people with IBD have abnormal depression scores (22.3% in the current study), this seems an important area of focus for future research, and we are currently exploring the effects of continuous and interval-type aerobic exercise training on physical fitness, fatigue, mental well-being and disease activity in people with inactive or mildly-active CD (26). Future studies, are also needed to better understand the sources of the unexplained variance in physical activity. Such studies should ideally be prospective, include objective measurement of physical activity, and include a range of intrapersonal, social and physical environmental predictor variables.

Few studies have explored the physical activity habits and limitations of people with IBD (10, 12, 13), but such information has practical value in the promotion of physical activity in this population. In this study, walking was the most common form of physical activity that the respondents participated in within the last year. Indeed, 57% of respondents cited walking, whereas the next most common activities of cycling, running, swimming, and gym were each cited by less than 20% of respondents. This finding is consistent with previous research that has demonstrated walking to be the most

common recreational and sporting activity undertaken by the general adult population (27) and people with IBD (10, 12). Health promotion initiatives seeking to engage people with IBD in physical activity need to be sensitive to the preferred mode of physical activity when designing interventions. Achieving a better understanding of physical activity *levels* may also represent a meaningful step in health promotion efforts in this population. Although 83% of all respondents indicated having undertaken one or more forms of physical activity in the last year, the IPAQ data showed that the same proportion (i.e., 83%) was classified as either "minimally-active" or "inactive". When compared against the results of the International Prevalence Study on Physical Activity (28), which also used the IPAQ short form to quantify physical activity levels, our findings suggest that people with IBD (and particularly those with more highly-active disease) are substantially less physically active than the general adult population. For example, 17% of our survey respondents were in the high physical activity category versus 62% of adults aged 18-65 years in the USA (28). The reasons for this are not fully understood, but might at least be partly explained by the fact that many people reported experiencing IBD-related limitations to physical activity such as pain, fatigue, disease flare-up and increased toilet urgency. Further research is needed to better understand the extent to which physical activity barriers and facilitators differ among specific sub-groups (e.g., CD versus UC/IC; active disease versus inactive disease), as this will assist in the design and tailoring of physical activity interventions.

A secondary objective of this study was to explore clinical and psychological correlates of fatigue. Fatigue is very common in IBD (29, 30). It is often associated with increased disease activity, pain, poor sleep quality, depression, and perceived stress (31). In the present study, fatigue was most prevalent in those with CD, females, those with high disease activity and those reporting lower levels of physical activity. Similar differences in prevalence of fatigue between CD and UC, gender and disease activity have been previously observed in a longitudinal study which, like ours, drew attention to patients with CD suffering more severe fatigue than those with UC, females being more

prone to it than males and fatigue levels increasing in line with disease severity (32). Another longitudinal study examined factors reducing fatigue and noted that regular exercise improved physical fatigue (33), corroborating our finding of fatigue being more prevalent in those reporting low levels of physical activity. In terms of predictors of fatigue, our adjusted models showed that both in CD and UC, anxiety and depression were associated with fatigue, which is consistent with the two previous longitudinal studies (32, 33) and the previous cross-sectional data summarised in a recent review (34). Graff et al. (32) explained this association by common pathways, and particularly pro-inflammatory cytokines contributing to mood changes, inflammation and fatigue, and neuroendocrine factors linking stress, inflammation and fatigue. Further, Graff et al. (32) also noticed that fatigue increases over time in IBD and that this process appears to be independent of disease activity, as some patients with inactive IBD also report significant levels of fatigue. In the present study, we observed a relationship between duration of illness (indicated by time since diagnosis) and fatigue in patients with CD. It is unclear why the same was not found in our participants with UC as that's contrary to previous observations. Further to this, disease activity predicted fatigue in CD and not UC. This perhaps could be explained by generally lower levels of fatigue reported in UC. Interestingly, at the multivariable level, female gender explained fatigue in UC but not in CD. Females in general report higher levels of fatigue than males (35). The fact that gender did not predict fatigue in CD may thus have more to do with our sample (predominantly female) than the actual differences between CD and UC. These predictors of fatigue, and particularly anxiety and depression which we identified as common for both CD and UC, may suggest that therapies targeting mental symptoms may be useful in also addressing fatigue comorbid with IBD. Solution-focused therapy has shown promise (36), however there are very few interventional studies in the area and more needs to be done to propose effective therapies for fatigue in IBD.

The strengths of this study include the use of a large clinically- and demographically-diverse sample and the exploration of a broad range of factors pertaining to physical activity. The limitations of this

study also need to be acknowledged. Firstly, as the data are cross-sectional, we cannot confirm the direction of relationships between physical activity, fatigue, and other disease and psychological variables. Secondly, the results might be prone to bias due to the exclusive use of self-reported data. For example, physical activity levels may have been under- or over-reported, and peoples' disease activity may have been incorrectly categorised. Thirdly, the fact that participants for this survey were self-selected and predominantly recruited via social network advertisements means that the results might not be directly generalisable to the wider IBD population. Of particular note, around 75% of respondents were female meaning that the results might not be directly relevant to males.

In summary, this large online survey has shown that the majority of respondents with IBD have low levels of physical activity. Associated factors included depression, disease activity and perceived barriers to exercise. A large proportion of respondents cited IBD-related limitations to physical activity such as pain, fatigue and increased toilet urgency. Given that regular physical activity may have numerous general and condition-specific benefits in people with IBD, attempting to increase participation of the IBD population in this vital health behaviour is probably a worthwhile pursuit. The results highlight several important factors that should be considered by designers of physical activity interventions for this population. Further research is now needed to better understand the barriers and facilitators of physical activity in specific sub-groups of patients, to determine the effects of different exercise programmes on important outcomes (e.g., fatigue, disease activity, and mental well-being), and to identify cost-effective interventions that have good potential for widespread implementation. Such efforts will help pave the way for the development of evidence-based physical activity guidelines for people with IBD.

Author Contributions

KJ and GT contributed to the design of the survey. KJ collated the results and conducted the analyses under the supervision of AMW and GT. All authors interpreted the data. GT drafted the manuscript.

KJ and AMW contributed to revising this report and gave final approval for its submission. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

References

1. Milanović Z, Sporiš G, Weston M. Effectiveness of High-Intensity Interval Training (HIT) and Continuous Endurance Training for VO2max Improvements: A Systematic Review and Meta-Analysis of Controlled Trials. Sports Med. 2015;45(10):1469-81.
2. Cooney GM, Dwan K, Greig CA, Lawlor DA, Rimer J, Waugh FR, et al. Exercise for depression. Cochrane Database Syst Rev. 2013(9):CD004366.
3. Verheggen RJ, Maessen MF, Green DJ, Hermus AR, Hopman MT, Thijssen DH. A systematic review and meta-analysis on the effects of exercise training versus hypocaloric diet: distinct effects on body weight and visceral adipose tissue. Obes Rev. 2016;17(8):664-90.
4. Fishman EI, Steeves JA, Zipunnikov V, Koster A, Berrigan D, Harris TA, et al. Association between Objectively Measured Physical Activity and Mortality in NHANES. Med Sci Sports Exerc. 2016;48(7):1303-11.
5. Bilski J, Mazur-Bialy A, Brzozowski B, Magierowski M, Zahradnik-Bilska J, Wójcik D, et al. Can exercise affect the course of inflammatory bowel disease? Experimental and clinical evidence. Pharmacol Rep. 2016;68(4):827-36.
6. D'Incà R, Varnier M, Mestriner C, Martines D, D'Odorico A, Sturniolo GC. Effect of moderate exercise on Crohn's disease patients in remission. Ital J Gastroenterol Hepatol. 1999;31(3):205-10.
7. Ng V, Millard W, Lebrun C, Howard J. Low-intensity exercise improves quality of life in patients with Crohn's disease. Clin J Sport Med. 2007;17(5):384-8.
8. Sharma P, Poojary G, Vélez DM, Dwivedi SN, Deepak KK. Effect of Yoga-Based Intervention in Patients with Inflammatory Bowel Disease. Int J Yoga Therap. 2015;25(1):101-12.
9. Klare P, Nigg J, Nold J, Haller B, Krug AB, Mair S, et al. The impact of a ten-week physical exercise program on health-related quality of life in patients with inflammatory bowel disease: a prospective randomized controlled trial. Digestion. 2015;91(3):239-47.
10. Mack DE, Wilson PM, Gilmore JC, Gunnell KE. Leisure-time physical activity in Canadians living with Crohn disease and ulcerative colitis: population-based estimates. Gastroenterol Nurs. 2011;34(4):288-94.
11. van Langenberg DR, Papandony MC, Gibson PR. Sleep and physical activity measured by accelerometry in Crohn's disease. Aliment Pharmacol Ther. 2015;41(10):991-1004.
12. DeFilippis EM, Tabani S, Warren RU, Christos PJ, Bosworth BP, Scherl EJ. Exercise and Self-Reported Limitations in Patients with Inflammatory Bowel Disease. Dig Dis Sci. 2016;61(1):215-20.
13. Chan D, Robbins H, Rogers S, Clark S, A P. Inflammatory bowel disease and exercise: results of a Crohn’s and Colitis UK survey Frontline Gastroenterology. 2014;5:44-8.
14. Neuendorf R, Harding A, Stello N, Hanes D, Wahbeh H. Depression and anxiety in patients with Inflammatory Bowel Disease: A systematic review. J Psychosom Res. 2016;87:70-80.
15. McKellar JD, Humphreys K, Piette JD. Depression increases diabetes symptoms by complicating patients' self-care adherence. Diabetes Educ. 2004;30(3):485-92.
16. Khanna R, Zou G, D'Haens G, Feagan BG, Sandborn WJ, Vandervoort MK, et al. A retrospective analysis: the development of patient reported outcome measures for the assessment of Crohn's disease activity. Aliment Pharmacol Ther. 2015;41(1):77-86.
17. Bennebroek Evertsz' F, Nieuwkerk PT, Stokkers PC, Ponsioen CY, Bockting CL, Sanderman R, et al. The patient simple clinical colitis activity index (P-SCCAI) can detect ulcerative colitis (UC) disease activity in remission: a comparison of the P-SCCAI with clinician-based SCCAI and biological markers. J Crohns Colitis. 2013;7(11):890-900.
18. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta Psychiatr Scand. 1983;67(6):361-70.
19. Czuber-Dochan W, Norton C, Bassett P, Berliner S, Bredin F, Darvell M, et al. Development and psychometric testing of inflammatory bowel disease fatigue (IBD-F) patient self-assessment scale. J Crohns Colitis. 2014;8(11):1398-406.

20. Craig CL, Marshall AL, Sjöström M, Bauman AE, Booth ML, Ainsworth BE, et al. International physical activity questionnaire: 12-country reliability and validity. Med Sci Sports Exerc. 2003;35(8):1381-95.
21. Sechrist KR, Walker SN, Pender NJ. Development and psychometric evaluation of the exercise benefits/barriers scale. Res Nurs Health. 1987;10(6):357-65.
22. Lysy Z, Da Costa D, Dasgupta K. The association of physical activity and depression in Type 2 diabetes. Diabet Med. 2008;25(10):1133-41.
23. Williams JW, Katon W, Lin EH, Nöel PH, Worchel J, Cornell J, et al. The effectiveness of depression care management on diabetes-related outcomes in older patients. Ann Intern Med. 2004;140(12):1015-24.
24. Lin EH, Katon W, Rutter C, Simon GE, Ludman EJ, Von Korff M, et al. Effects of enhanced depression treatment on diabetes self-care. Ann Fam Med. 2006;4(1):46-53.
25. Azevedo Da Silva M, Singh-Manoux A, Brunner EJ, Kaffashian S, Shipley MJ, Kivimäki M, et al. Bidirectional association between physical activity and symptoms of anxiety and depression: the Whitehall II study. Eur J Epidemiol. 2012;27(7):537-46.
26. Tew GA, Carpenter R, Seed M, Anderson S, Langmead L, Fairhurst C, et al. Feasibility of high-intensity interval training and moderate-intensity continuous training in adults with inactive or mildly active Crohn's disease: Study protocol for a randomised controlled trial BMC Gastroenterology. in review.
27. Bryan SN, Katzmarzyk PT. Patterns and trends in walking behaviour among Canadian adults. Can J Public Health. 2009;100(4):294-8.
28. Bauman A, Bull F, Chey T, Craig CL, Ainsworth BE, Sallis JF, et al. The International Prevalence Study on Physical Activity: results from 20 countries. Int J Behav Nutr Phys Act. 2009;6:21.
29. Minderhoud IM, Oldenburg B, van Dam PS, van Berge Henegouwen GP. High prevalence of fatigue in quiescent inflammatory bowel disease is not related to adrenocortical insufficiency. Am J Gastroenterol. 2003;98(5):1088-93.
30. Graff LA, Vincent N, Walker JR, Clara I, Carr R, Ediger J, et al. A population-based study of fatigue and sleep difficulties in inflammatory bowel disease. Inflamm Bowel Dis. 2011;17(9):1882-9.
31. Graff LA, Walker JR, Russell AS, Bissonnette R, Bernstein CN. Fatigue and quality of sleep in patients with immune-mediated inflammatory disease. J Rheumatol Suppl. 2011;88:36-42.
32. Graff LA, Clara I, Walker JR, Lix L, Carr R, Miller N, et al. Changes in fatigue over 2 years are associated with activity of inflammatory bowel disease and psychological factors. Clin Gastroenterol Hepatol. 2013;11(9):1140-6.
33. van Langenberg DR, Gibson PR. Factors associated with physical and cognitive fatigue in patients with Crohn's disease: a cross-sectional and longitudinal study. Inflamm Bowel Dis. 2014;20(1):115-25.
34. Artom M, Czuber-Dochan W, Sturt J, Norton C. Targets for Health Interventions for Inflammatory Bowel Disease-fatigue. J Crohns Colitis. 2016;10(7):860-9.
35. Schwarz R, Krauss O, Hinz A. Fatigue in the general population. Onkologie. 2003;26(2):140-4.
36. Vogelaar L, van't Spijker A, Timman R, van Tilburg AJ, Bac D, Vogelaar T, et al. Fatigue management in patients with IBD: a randomised controlled trial. Gut. 2014;63(6):911-8.

440 **Figure Legends**

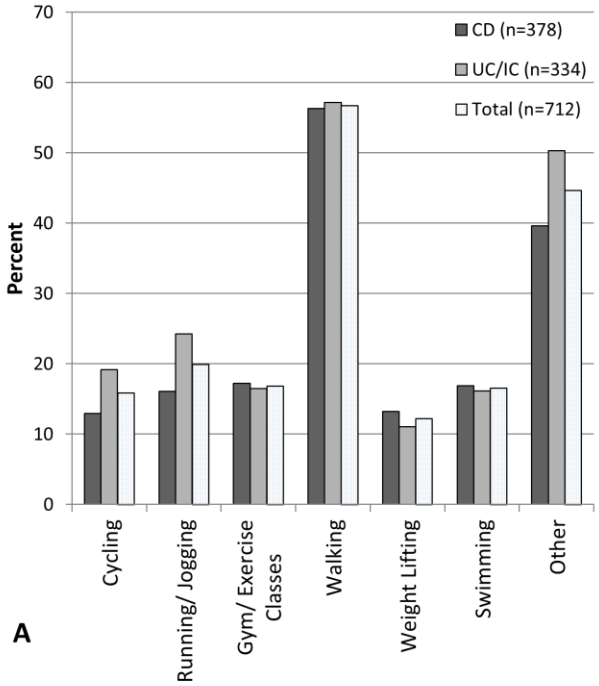
441 **Figure 1** The most common types of physical activity/exercise that respondents participated

442 in during the last year (Panel A) and avoided because of IBD (Panel B)

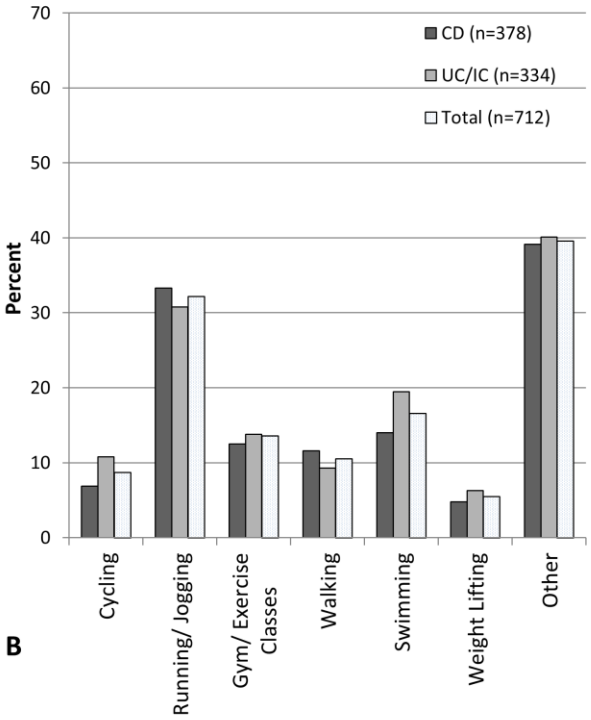
443 **Figure 2** Reasons given for IBD limiting participation in physical activity/exercise

444 **Figure 3** Average fatigue levels in the past two weeks (values in bars are %)

445

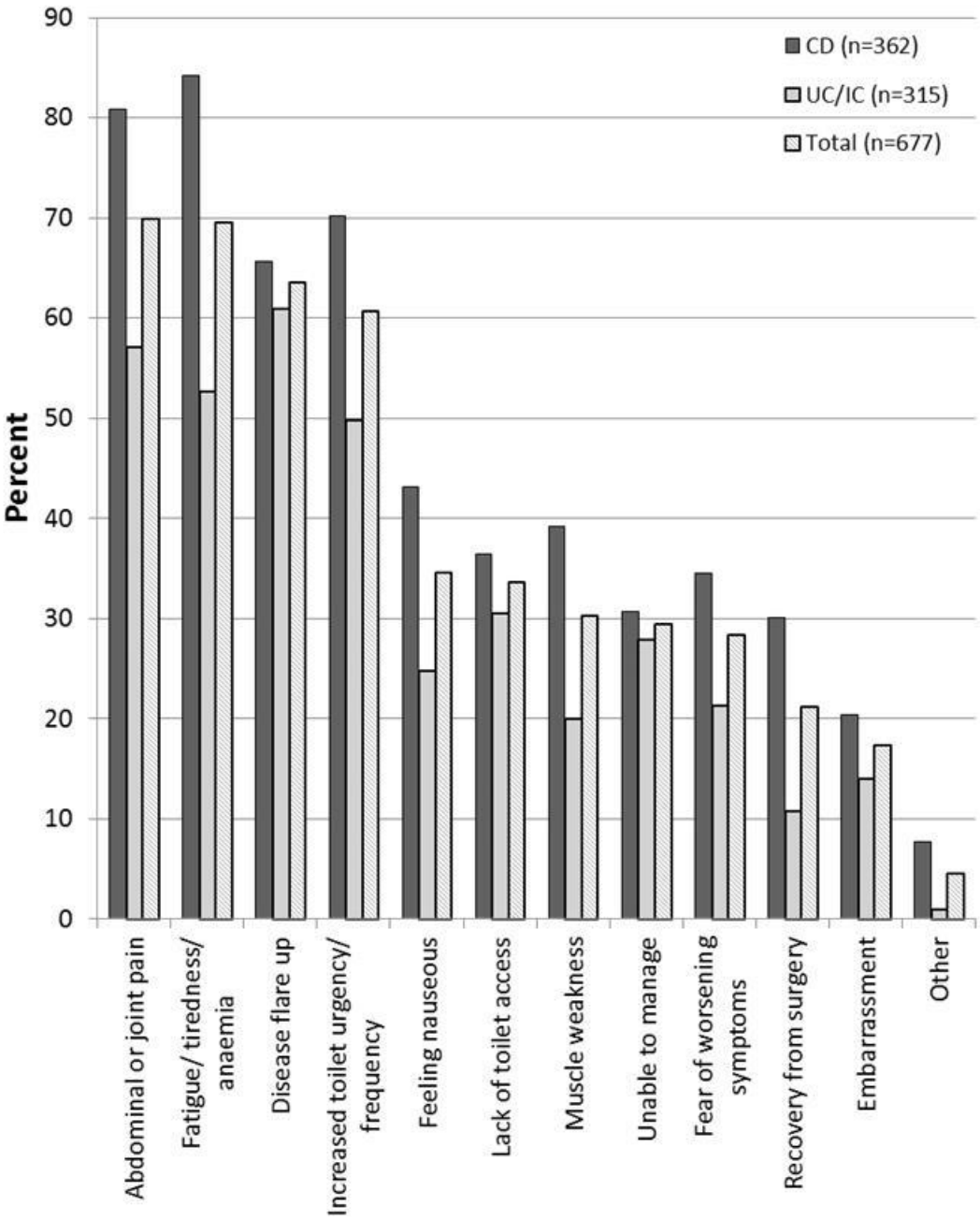

70
60
50
40
30
20
10
0
Percent
CD (n=378)
UC/IC (n=334)
Total (n=712)
Cycling
Running/ Jogging
Gym/ Exercise Classes
Walking
Weight Lifting
Swimming
Other
A

446


70
60
50
40
30
20
10
0
Percent
CD (n=378)
UC/IC (n=334)
Total (n=712)
Cycling
Running/ Jogging
Gym/ Exercise Classes
Walking
Swimming
Weight Lifting
Other
B

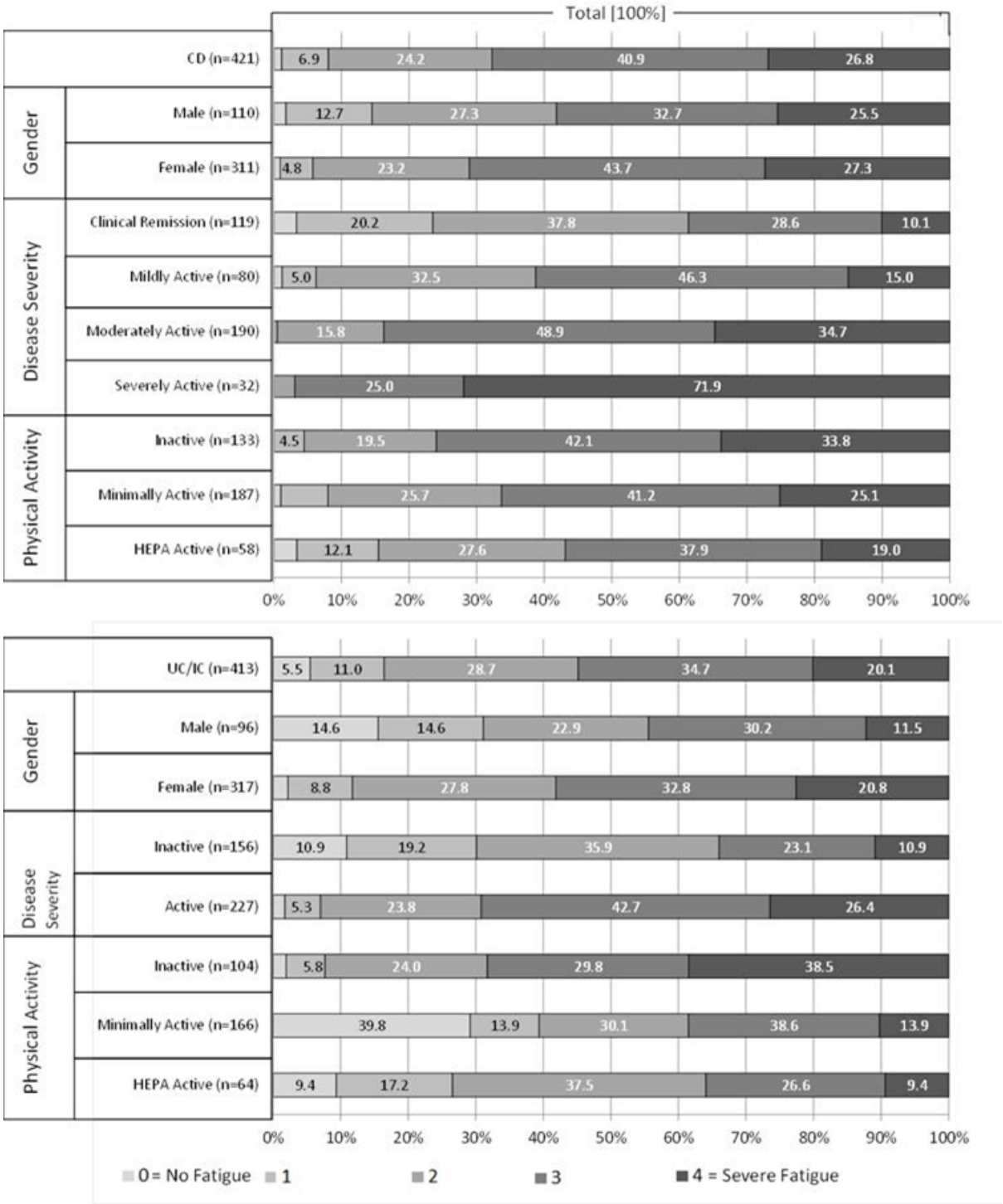
447

448


Percent
90
80
70
60
50
40
30
20
10
0
CD (n=362)
UC/IC (n=315)
Total (n=677)
Abdominal or joint pain
Fatigue/ tiredness/ anaemia
Disease flare up
Increased toilet urgency/ frequency
Feeling nauseous
Lack of toilet access
Muscle weakness
Unable to manage
Fear of worsening symptoms
Recovery from surgery
Embarrassment
Other

449

450


Total [100%]
CD (n=421)
6.9
24.2
40.9
26.8
Gender
Male (n=110)
12.7
27.3
32.7
25.5
Female (n=311)
4.8
23.2
43.7
27.3
Disease Severity
Clinical Remission (n=119)
20.2
37.8
28.6
10.1
Mildly Active (n=80)
5.0
32.5
46.3
15.0
Moderately Active (n=190)
15.8
48.9
34.7
Severely Active (n=32)
25.0
71.9
Physical Activity
Inactive (n=133)
4.5
19.5
42.1
33.8
Minimally Active (n=187)
25.7
41.2
25.1
HEPA Active (n=58)
12.1
27.6
37.9
19.0
0%
10%
20%
30%
40%
50%
60%
70%
80%
90%
100%
UC/IC (n=413)
5.5
11.0
28.7
34.7
20.1
Gender
Male (n=96)
14.6
14.6
22.9
30.2
11.5
Female (n=317)
8.8
27.8
32.8
20.8
Disease Severity
Inactive (n=156)
10.9
19.2
35.9
23.1
10.9
Active (n=227)
5.3
23.8
42.7
26.4
Physical Activity
Inactive (n=104)
5.8
24.0
29.8
38.5
Minimally Active (n=166)
39.8
13.9
30.1
38.6
13.9
HEPA Active (n=64)
9.4
17.2
37.5
26.6
9.4
0%
10%
20%
30%
40%
50%
60%
70%
80%
90%
100%
0 = No Fatigue
1
2
3
4 = Severe Fatigue

451

452 **Table 1** Demographic and disease-related characteristics

	CD (n = 446)	UC/IC (n = 413)	Total (n = 859)
Age, mean (SD), years	36.9 (11.5)	37.7 (11.6)	37.3 (11.6)
Female, n (%)	329 (73.8)	317 (76.8)	646 (75.2)
Male, n (%)	117 (26.2)	96 (23.2)	213 (24.8)
Employment status, n (%)			
Employed Full Time	192 (43.0)	232 (56.2)	424 (49.4)
Employed Part Time	70 (15.7)	60 (14.5)	130 (15.1)
Unemployed- Unable	83 (18.6)	39 (9.4)	122 (14.2)
Unemployed- Other	32 (7.2)	25 (6.1)	57 (6.6)
Student	55 (12.3)	36 (8.7)	91 (10.6)
Retired	11 (2.6)	17 (4.1)	28 (3.3)
Don’t know/ Prefer not to say	3 (0.7)	4 (1.0)	7 (0.8)
Smoking Status, n (%)			
Yes	75 (16.8)	33 (8.0)	108 (12.6)
No	278 (62.3)	293 (70.9)	571 (66.5)
Not anymore	92 (20.6)	86 (20.8)	178 (20.7)
Don’t Know/ Prefer not to say	1 (0.2)	1 (0.2)	2 (0.2)
Time since diagnosis, median (IQR), months[a]	102 (36-188)	74.5 (36-168)	87 (36-178)
Disease activity, n (%)[a]			
PRO3: Clinical Remission	119 (28.3)		
PRO3: Mildly Active	80 (19.0)		
PRO3: Moderately Active	190 (45.1)		
PRO3: Severely Active	32 (7.6)		

P-SCCAI: Inactive	156 (40.7)
P-SCCAI: Active	227 (59.3)

CD, Crohn's Disease; UC, Ulcerative Colitis; IC, Indeterminate Colitis; PRO3, 3-item Patient Reported Outcome (CD only); P-SCCAI, Patient-based Simple Clinical Colitis Activity Index (UC/IC only)

[a]5.6% (n = 25) CD respondents and 7.3% (n = 30) UC/IC respondents did not complete

457 **Table 2** Clinical characteristics

	CD (n = 421)	UC/IC (n = 383)	Total (n = 804)
Current Treatment (%)[a]			
Oral 5-Aminosalicytes	95 (23.3)	196 (54.0)	291 (37.9)
Corticosteroids	83 (20.4)	79 (21.7)	162 (21.0)
Immunosuppressants	262 (63.7)	147 (38.6)	409 (51.7)
Antibiotics	23 (5.5)	17 (4.4)	40 (4.9)
Anti-Diarrheals	83 (19.7)	71 (18.5)	154 (19.2)
Pain Relief	163 (38.7)	99 (26.1)	262 (32.7)
Iron Supplements	85 (20.2)	67 (17.5)	152 (18.9)
Vitamin B-12 Injections	111 (26.4)	N/A	111 (13.8)
Calcium Supplements	94 (22.3)	N/A	94 (11.7)
Vitamin D Supplements	139 (33.0)	N/A	139 (17.3)
Nutrition Therapy	15 (3.6)	N/A	15 (1.9)
No Medication Required	20 (4.8)	27 (7.3)	47 (6.0)
Don’t Know/ Prefer not to say	3 (0.7)	5 (1.3)	8 (1.0)
Other	66 (15.7)	62 (16.2)	128 (15.9)
Surgical History (%)[a]			
Permanent Ileostomy	27 (6.4)	27 (7.0)	54 (6.7)
Temporary Ileostomy	38 (9.0)	43 (11.2)	81 (10.1)
Permanent Colostomy	13 (3.1)	29 (7.6)	42 (5.2)
Temporary Colostomy	7 (1.7)	3 (0.8)	10 (1.2)
Strictureplasty	24 (5.7)	N/A	24 (3.0)
Resection	111 (26.4)	N/A	111 (13.8)

Ileocaecal Resection	49 (11.6)	N/A	49 (6.1)
Limited Right Hemicolectomy	32 (7.6)	N/A	32 (4.0)
Proctocolectomy	15 (3.6)	N/A	15 (1.9)
Ileo-Anal Pouch	N/A	54 (14.1)	54 (6.7)
I have not had surgery	203 (48.2)	283 (73.9)	486 (60.4)
Don't know/ Prefer not to say	2 (0.5)	1 (0.3)	3 (0.4)
Other	62 (14.7)	21 (5.5)	83 (10.3)
Time Since Last Surgery, median (IQR), months	36 (16-96)	36 (12-84)	36 (13-84)

458 CD, Crohn's Disease; UC, Ulcerative Colitis; IC, Indeterminate Colitis

459 [a]5.6% (n = 25) CD respondents and 7.3% (n = 30) UC/IC respondents did not complete

Table 3 Physical activity, depression and anxiety data by disease type and activity

	Total (n = 834)	CD (n = 421)				UC/IC (n = 413)	
		Clinical remission	Mildly active	Moderately active	Severely active	Inactive	Active
IPAQ Category (%)[a]							
HEPA active	17.1	21.5	23.2	10.4	3.4	21.2	17.8
Minimally active	49.6	51.4	55.1	48.6	34.5	57. 6	44.1
Inactive	33.3	27.1	21.7	41.0	62.1	21.2	38.1
IPAQ MVPA, median (IQR),	360	960	720	0	0	820	120
MET·min/week[a]	(0-1875)	(0-2120)	(0-2040)	(0-1380)	(0-410)	(0-2160)	(0-1440)
IPAQ Total PA, median (IQR),	1866	2222	2730	1386	600	2355	1386
MET·min/week[ab]	(594-4040)	(1205-4584)	(1158-4986)	(996-3412)	(60-2079)	(983-4650)	(446-3465)
IPAQ Sitting, mean (SD), min/day[a]	429 (225)	369 (177)	416 (220)	444 (254)	561 (317)	410 (202)	445 (214)
EBBS Barriers Score, mean (SD)[c]	31.6 (6.6)	29.8 (7.0)	31.5 (6.6)	33.4 (5.4)	34.2 (7.0)	30.2 (6.4)	31.7 (6.8)
EBBS Benefits Score, mean (SD) [c]	84.9 (15.3)	87.8 (14.3)	83.0 (20.3)	81.2 (13.6)	80.1 (15.8)	88.0 (15.0)	86.4 (14.9)

HADS Anxiety, mean (SD)	9.1 (4.5)	7.3 (4.1)	8.9 (4.3)	11.4 (4.1)	12.4 (3.7)	6.8 (4.1)	9.6 (4.3)
HADS Depression, mean (SD)	7.0 (4.3)	4.8 (3.4)	6.7 (4.2)	9.2 (4.1)	11.3 (3.7)	4.5 (3.5)	7.8 (4.1)

CD, Crohn's Disease; UC, Ulcerative Colitis; IC, Indeterminate Colitis; IPAQ, International Physical Activity Questionnaire; EBBS, Exercise Benefits/Barriers Scale; HADS, Hospital Anxiety and Depression Scale; MVPA, Moderate-to-Vigorous Physical Activity

[a]10.2% (n = 43) CD respondents and 19% (n = 79) UC/IC respondents did not complete

[b]Total physical activity computed as the sum of Walking + Moderate + Vigorous MET·min/week scores

[c]14% (n = 59) CD respondents and 23.7% (n = 98) UC/IC respondents did not complete

Table 4 Correlation matrix between physical activity and fatigue (composite) scores and various demographic, clinical and psychological factors

	Physical activity[a]		Fatigue	
	CD	UC/IC	CD	UC/IC
Age	-0.098	-0.158**	0.036	-0.070
Time since diagnosis	-0.042	-0.064	0.110*	0.017
Disease activity	-0.228**	-0.123*	0.479**	0.393**
Depression	-0.287**	-0.240**	0.538**	0.572**
Anxiety	-0.120*	0.049	0.465**	0.453**
Physical activity	-	-	-0.127*	-0.181**
Fatigue	-0.127*	-0.181**	-	-
Exercise benefits	0.244**	0.171**	N/A	N/A
Exercise barriers	-0.292**	-0.112	N/A	N/A

CD, Crohn's disease; IC, Indeterminate Colitis; UC, Ulcerative Colitis

[a]Total physical activity computed as the sum of Walking + Moderate + Vigorous MET·min/week scores (logarithmic transformed)

*Correlation is significant at the 0.05 level

**Correlation is significant at the 0.01 level

Table 5 Regression model results for total physical activity (logarithmic transformed)

	Crohn's Disease						Ulcerative and Indeterminate Colitis					
	B	Std. Error	Beta	t	P-value	Adjusted R^2	B	Std. Error	Beta	t	P-value	Adjusted R^2
First Model[a]												
(Constant)	8.015	0.862		9.299	<0.001	0.132	7.685	0.609		12.611	<0.001	0.076
Age	N/A	N/A	N/A	N/A	N/A		-0.016	0.006	-0.146	-2.566	0.011	
Gender	0.216	0.155	0.074	1.393	0.165		0.000	0.168	0.097	1.676	0.095	
Disease activity	-0.010	0.005	-0.130	-2.083	0.038		-0.053	0.027	-0.001	-0.010	0.992	
Depression	-0.077	0.024	-0.251	-3.199	0.002		-0.053	0.024	-0.177	-2.252	0.025	
Anxiety	0.034	0.021	0.114	1.576	0.116		N/A	N/A	N/A	N/A	N/A	
Fatigue	0.024	0.018	0.086	1.294	0.197		-0.013	0.019	-0.049	-0.671	0.503	
Exercise benefits	0.007	0.006	0.081	1.238	0.216		0.005	0.005	0.062	0.993	0.321	
Exercise barriers	-0.035	0.013	-0.171	-2.655	0.008		N/A	N/A	N/A	N/A	N/A	
Second Model[b]												
(Constant)	9.437	0.342		27.563	<0.001	0.123	8.505	0.247		34.439	<0.001	0.073

Age	N/A	N/A	N/A	N/A	N/A	-0.015	0.006	-0.145	-2.636	0.009
Disease activity	-0.009	0.005	-0.109	-1.873	0.062	N/A	N/A	N/A	N/A	N/A
Depression	-0.048	0.019	-0.157	-2.563	0.011	-0.069	0.016	-0.232	-4.216	<0.001
Exercise barriers	-0.043	0.011	-0.212	-3.847	<0.001	N/A	N/A	N/A	N/A	N/A

[a]Including only those variables that were significantly correlated with physical activity in the initial exploratory work (correlation matrices)

[b]Including only those variables that were statistically significant in the First Model

Table 6 Regression model results for fatigue (composite score)

	Crohn's Disease						Ulcerative and Indeterminate Colitis					
	B	Std. Error	Beta	t	P-value	Adjusted R^2	B	Std. Error	Beta	t	P-value	Adjusted R^2
First Model[a]												
(Constant)	0.380	1.549		0.245	0.806	0.367	4.512	1.547		2.917	0.004	0.373
Gender	-0.649	0.473	-0.062	-1.373	0.171		-1.360	0.495	-0.125	-2.744	0.006	
Time since diagnosis	0.005	0.002	0.112	2.550	0.011		N/A	N/A	N/A	N/A	N/A	
Disease activity	0.083	0.014	0.287	5.772	<0.001		0.152	0.081	0.098	1.884	0.061	
Depression	0.278	0.070	0.251	3.982	<0.001		0.454	0.070	0.408	6.455	<0.001	
Anxiety	0.226	0.063	0.211	3.554	<0.001		0.180	0.061	0.172	2.969	0.003	
Physical activity	0.163	0.163	0.045	0.996	0.320		-0.253	0.180	-0.068	-1.405	0.161	
Second Model[b]												
(Constant)	1.172	0.503		2.328	0.020	0.370	3.320	0.727		4.565	<0.001	0.360
Gender	N/A	N/A	N/A	N/A	N/A		-1.476	0.455	-0.133	-3.242	0.001	

Time since diagnosis	0.003	0.002	0.083	2.111	0.035	N/A	N/A	N/A	N/A	N/A
Disease activity	0.076	0.013	0.270	6.102	<0.001	N/A	N/A	N/A	N/A	N/A
Depression	0.324	0.060	0.295	5.375	<0.001	0.517	0.057	0.465	9.148	<0.001
Anxiety	0.183	0.056	0.170	3.237	0.001	0.178	0.054	0.168	3.312	0.001

[a]Including only those variables that were significantly correlated with fatigue in the initial exploratory work (correlation matrices)

[b]Including only those variables that were statistically significant in the First Model